REMARKS

The Claims

Claims 58-68 are currently pending in the application.

Claim 58 has been amended to recite a method for "determining a decrease in the activity of osteoprotegerin binding protein (OPGbp) comprising adding a compound to an in vitro assay...". Support for the amended claim is found at p. 23, lines 22-35; p. 26, lines 29-35 and p. 27, line 5 to p. 30, line 7 of the specification.

Claims 60 and 64 have been cancelled without prejudice or disclaimer.

Claims 71 to 73 have been added. Support for the new claims is found at p. 19, lines 28-35.

Upon entry of the amendments, Claims 58, 59, 61-63, 65-68 and 71-73 will be pending in the application.

Abstract of the Invention

The abstract is objected to as it allegedly does not disclose the claimed invention which the Examiner considers to be the method of Claim 58. Upon an indication of allowable subject matter, Applicant will amend the abstract accordingly.

Information Disclosure Statement

Applicant submits herewith a Supplemental Information Disclosure Statement and SB08 Form and requests that the references set forth therein be considered and made of record in the present application.

Rejections under 35 U.S.C. 112

The rejection of Claims 58-62 and 64-68 under 35 U.S.C. 112, first paragraph, has been maintained. The Examiner's main arguments may be summarized as follows:

The present claims encompass use of in vivo assays and unspecified assays whereas original Claim 43 was limited to an in vitro method.

A passage of the specification at p. 23 cited by Applicant as support for the claimed invention is alleged to be limited to an in vitro method for measuring OPGbp/ligand binding. The passage is also alleged to include an additional step wherein the compound is assayed for agonist or antagonist activity, but there is no description as to how said activity is measured.

It is alleged that Claim 62 lacks written description because original claim 43 is limited to a method wherein osteoclast formation is measured in a cell culture.

A passage of the specification at p. 30 cited by Applicant as support for the claimed invention is alleged to be limited to compounds which decrease the interaction of OPGbp and ODAR, wherein the present claims are not so limited. The cited passage is also alleged to be limited to certain in vivo assays whereas the claimed invention is not.

Original Claim 29 in U.S. Serial No. 09/052,521 is alleged to not be drawn to the same claimed invention because it does not claim the additional method steps of Claim 58.

Applicant traverses the rejection. Present Claim 58 and claims depending therefrom are fully supported by the specification and that no new matter has been introduced. As pointed out by Applicant in his response mailed September 4, 2008, the specification discloses a variety of in vitro and in vivo assays that may be used to determine the interaction of OPG binding protein (hereafter "OPGbp") with ODAR and to measure OPGbp activity.

The specification makes clear that OPG binding protein activity includes the stimulation of osteoclast formation and bone resorption which is the result of the interaction of OPGbp with ODAR:

> Osteoclast development and the rate and extent of bone resorption are regulated by the interaction of OPG binding protein and ODAR. Compounds which decrease or block the interaction of OPG binding protein and ODAR are potential antagonists of OPG binding protein activity and may disrupt osteoclast development leading to decreased bone resorption. (specification at p. 26, lines 29-35)

The paragraph also makes clear that an antagonist of OPGbp activity can decrease osteoclast formation and bone resorption.

A number of examples of in vitro assays for measuring the interaction of OPGbp and ODAR are described starting on p. 27, line 5. These assays employ radiolabeling, enzyme-linked colorimetric detection or fluorescent tagging to measure binding. Surface plasmon resonance detection, such as BIAcore, is also disclosed. Cell-based assays are described starting on p. 29, line 22, and may be used to not only detect binding of OPGbp to ODAR but also to measure OPG binding activity using appropriate cell lines as taught in the specification. Example 8 provides additional detail on one such cell based assay and refers to another published assay at p. 49, lines 17-21.

An example of in vivo evaluation of compounds which decrease the interaction of OPGbp and ODAR and decrease the activity of OPGbp is described in the specification as follows:

> Compounds which increase or decrease the interaction of OPG binding protein with ODAR may also be evaluated for in vivo activity by administration of the compounds to mice followed by measurement of bone density using bone scanning densitometry or radiography. Procedures for measuring bone density are described in PCT publication WO 97/23614 and in Example 13. (specification at p. 30, lines 8-15.)

In order to satisfy the written description requirement under 35 U.S.C. 112, "the applicant must ... convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention" *Vas-Cath, Inc. v. Mahurkar* 19 USPQ2d 1117 (Fed. Cir. 1991). The specification as a whole, and in particular those sections from p. 27, line 5 to p. 30, line 15 clearly convey that the

Applicant was in possession of the invention as claimed. The specification does not teach the skilled person that a particular assay must be used for determining OPGbp activity and, in fact, it does exactly the opposite by disclosing a number of different assays for measuring the effects of compounds on OPGbp activity.

None of the Examiner's arguments summarized above support the position that the claims lack adequate written description.

It is argued that original Claim 43 is limited to an in vitro method whereas Claims 58-62 and 64-68 encompass in vivo and unspecified assays. This argument is irrelevant as original Claim 443 has not been relied upon by Applicant for written description. As discussed above, support for the claims is found in the specification, for example starting at p. 27, line 5 to p. 30, line 15, as discussed above.

The Examiner alleges that a passage at p. 23 of the specification cited by Applicant is limited to an in vitro method, and also alleges that the passage includes an additional step of measuring agonist or antagonist activity without any description of how such activity is measured. The passage states:

> Methods for identifying compounds which interact with OPG binding protein are also encompassed by the invention. The method comprises incubating OPG binding protein with a compound under conditions which permit binding of the compound to OPG binding protein, and measuring the extent of binding. The compound may be substantially purified or present in a crude mixture. Binding compounds may be nucleic acids, proteins, peptides, carbohydrates, lipids or small molecular weight organic compounds. The compounds may be further characterized by their ability to increase or decrease OPG binding protein activity in order to determine whether they act as an agonist or an antagonist. (specification at p. 23, lines 22-35)

The Examiner has not established any basis for the assertion that this passage is limited to in vitro methods. In fact, no such limitation, either explicit or implicit, exists in the specification. Moreover, the specification discloses at p. 29, line 22 to p. 30, line 15 both in vitro and in vivo assays for determining whether a compound is an agonist or antagonist of OPGbp activity.

The Examiner argues that Claim 62 is not adequately supported because original Claim 43 is limited to a method wherein osteoclast formation is measured in a cell culture. The argument is irrelevant as Applicant is not relying on Claim 43 to satisfy the written description requirement. Measurement of osteoclast formation can be carried out by in vitro and in vivo methods disclosed in the specification at p. 29, line 22 to p. 30, line 15.

It is alleged that the passage in the specification at p. 30 cited by Applicant (lines 8-15 quoted above) is limited to compounds which decrease the interaction of OPGbp and ODAR, wherein the present claims encompass compounds which decrease the functional activity of OPGbp other than by decreasing the interaction between OPGbp and ODAR. The cited passage is also alleged to be limited to certain in vivo assays. Claim 58 is directed to a compound which binds to OPGbp and decreases the activity of OPGbp as determined by a decrease in osteoclast formation. The specification at p. 26, lines 29-35 states that compounds which decrease or block the interaction of OPGbp and ODAR are potential antagonists of OPGbp that may disrupt osteoclast development leading to decreased bone resorption.

The Examiner argues that original Claim 29 in U.S. Serial No. 09/052,521 (hereafter the "'521 application") does not support the claimed invention because it does not claim the additional method steps of Claim 58. Claim 29 of the '521 application reads as follows:

> A method to assess the ability of a candidate compound to bind to an osteoprotegerin binding protein comprising: incubating the osteoprotegerin binding protein with the candidate compound under conditions that allow binding; and measuring the bound compound.

Applicant's reference to Claim 29 of the '521 application was intended to point out that the first step of Claim 29, which is similar to the first step of present Claim 58, is not limited to in vitro methods. The Examiner has not asserted any basis in the specification for introducing such a limitation.

In summary, Applicant maintains that original Claim 58 as well as the claim in its presently amended form is fully supported by the specification. It is requested that the rejection be withdrawn.

The rejection of Claim 60 under 35 U.S.C. 112, first paragraph has been maintained. The claim recites a compound which binds to OPGbp and blocks binding of OPGbp to human ODAR. The Examiner argues that the specification does not provide adequate written description for the term "human ODAR" as the term would encompass human ODAR variants, mutants and alleles, none of which are allegedly disclosed in the specification.

Without acquiescing to the rejection and solely to advance prosecution, Applicant has cancelled Claim 60 without prejudice, thereby rendering the rejection moot.

Rejection under 35 U.S.C. 103

Claims 58-68 are rejected under 35 U.S.C. 103(a) as being unpatentable over Boyle (U.S. Patent No. 6,316,408) in view of Choi et al. (WO 02/16551). The Examiner argues that the '408 patent and WO 02/16551 may be properly cited as the claims of the present application are not allegedly not entitled to their priority dates in view of the rejections under 35 U.S.C. 112.

Applicant traverses the rejection. U.S. Patent 6,316,408 to Boyle (hereafter "the '408 patent") and the present application both claim priority from U.S. Serial No. 08/842,842 filed April 16, 1997. As explained above, the present claims are fully supported in the specification and are therefore entitled to their earliest priority date of April 16, 1997, thereby removing the '408 patent as a prior art reference under 35 U.S.C. 103(a). Choi et al. (PCT Publication No. WO 02/16551) was published on February 28, 2002, which is a date more than four years after the priority date of the present application, and is therefore not a prior art reference under 35 U.S.C. 103(a). Moreover, the skilled person could not have combined the disclosures of the '408

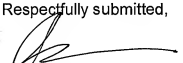
patent and WO 02/16551 before the priority date of the present application. Accordingly, neither the '408 patent nor WO 02/16551 can form the basis for a rejection under 35 U.S.C. 103(a). The rejection should be withdrawn.

CONCLUSION

It is believed that Claims 58, 59, 61-63, 65-68 and 71-73 are in condition for allowance and a notice thereof is solicited.

The Commissioner is hereby authorized to charge any additional fees, which may be required, or credit any overpayment to Deposit Account No. 01-0519.

Respectfully submitted,



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